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Pandemic Influenza: Domestic Preparedness Efforts

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Pandemic Influenza: Domestic Preparedness Efforts

Summary

In 1997, a new avian influenza virus (H5N1 avian flu) emerged in Hong Kong, killing six people. This was the first time that an avian influenza virus was shown to be transmitted directly from birds to humans. The virus persisted in the region, and has since spread to a number of Asian and European countries, where it has infected more than 120 people, killing more than 60. The severity of this strain is similar to that of the deadly 1918 Spanish flu, which caused a global pandemic that may have killed up to 2% of the world's population. Though influenza pandemics occur with some regularity, and the United States has been involved in specific planning efforts since the early 1990s, the H5N1 situation has created a sense of urgency among the world's public health officials.

Global pandemic preparedness and response efforts are coordinated by the World Health Organization (WHO). The U.S. Department of Health and Human Services (HHS) released a draft pandemic flu preparedness and response plan in August 2004, and a final plan in November 2005. President Bush announced a national strategy to coordinate pandemic preparedness and response activities across federal agencies. Domestic response activities will be carried out under the broad, all-hazards blueprint for a coordinated federal, state and local response laid out in the National Response Plan, released by the Department of Homeland Security (DHS) in 2004.

Even in light of the plans discussed above, if a flu pandemic were to occur in the next several years, the U.S. response would be affected by the limited availability of a vaccine (the best preventive measure for flu), as well as by limited availability of certain drugs used to treat severe flu infections, and by the general lack of surge capacity within our healthcare system. The U.S. healthcare system is largely private, while the public health system is largely based in state, rather than federal, authority. This structure creates numerous challenges in assuring the needed response capacity, and coordinating the various response elements. Planning is further complicated by the fact that while periodic influenza pandemics have been seen over the years, their timing and severity have been unpredictable. This report will be updated to reflect changing circumstances.

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Pandemic Influenza: Domestic Preparedness Efforts

Between pathogens and humans it is a race of their genes against our wits.

Joshua Lederberg, who won the 1958 Nobel Prize in Medicine for his work on genetic recombination in bacteria.

Introduction

In 1997 a new strain of influenza (flu) jumped from poultry directly to humans in Hong Kong, causing several human deaths. This was the first documented occurrence of direct transmission of an avian flu virus from birds to people. Despite efforts to contain the virus through mass culling of poultry flocks, the virus (also called H5N1 for specific proteins on its surface) re-emerged in 2003. It has since been reported in domestic poultry and/or migratory birds in more than a dozen Asian countries, and in Europe.¹ Also since 2003, it has infected more than 120 people in Cambodia, Indonesia, Thailand, and Vietnam, resulting in more than 60 deaths.² As of yet the virus has not developed the ability to transmit efficiently from person to person. Were that to occur, a global influenza pandemic would be likely.

The high lethality of the H5N1 strain and its tendency to affect healthy young people remind health authorities of the deadly 1918 Spanish flu, which is estimated to have killed up to 2% of the world's population, and was a substantial cause of mortality in U.S. military personnel in World War I. The World Health Organization (WHO) says, "If an influenza pandemic virus were to appear again similar to the one that struck in 1918, even taking into account the advances in medicine since then, unparalleled tolls of illness and death could be expected."³

U.S. and world health authorities believe that while periodic influenza pandemics are inevitable, their progress may be slowed, and their impacts blunted,

¹ World Organization for Animal Health (known by its French acronym, OIE), "Update on Avian Influenza in Animals in Asia (Type H5)," at [http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm]. OIE is an intergovernmental organization of 167 nations and is not part of the United Nations system.

² World Health Organization, "Confirmed Human Cases of Avian Influenza A/(H5N1)," as of Nov. 1, 2005, at [http://www.who.int/csr/disease/avian_influenza/country/en/].

³ WHO, "Global Influenza Preparedness Plan: The Role of WHO and Recommendations for National Measures before and during Pandemics," 2005, (hereafter called the WHO pandemic plan), p. 3, at [<http://www.who.int/csr/disease/influenza/pandemic/en/>].

by rapid detection and local control efforts. The added time would allow affected countries to better manage the situation, and countries not yet affected to better prepare. To realize these benefits, countries affected by avian flu must be able to track the spread of the virus in birds, and quickly detect and investigate suspected human cases. Hence, a country's capabilities in epidemiology, laboratory detection and other public health services affect the welfare of the global community as well as the country itself. This fact presents developed nations with novel policy challenges, such as whether to reserve scarce health resources such as antiviral drugs for themselves, or to deploy them to other countries at the center of an emerging pandemic.

WHO released a pandemic preparedness plan in early 2005, updated from its prior 1999 draft. The United States released a draft pandemic plan in August 2004, a national strategy on November 1, 2005, and a final plan on November 2, 2005. States were required to prepare pandemic plans as a condition of their federal bioterrorism preparedness grants. The sudden shortage of seasonal flu vaccine in the United States for the 2004-2005 season offered an unplanned mini-drill for pandemic preparedness, highlighting the implications of limited vaccine and antiviral production capacity and the absence of a coordinated federal/state/local/private distribution system for vaccine distribution. In a pandemic, vaccine would likely be federally owned and distributed through a national system designed to support the Strategic National Stockpile. But antiviral drugs would be controlled by a mix of federal, state, local and private holders, and its distribution would likely face the same challenges posed by the 2004 seasonal flu vaccine shortage.

A recurring theme in WHO planning documents and consultations is the need for countries to engage sectors beyond healthcare and public health in preparedness and response. On October 27, 2005, Health and Human Services (HHS) Secretary Michael Leavitt said, "If a pandemic hits our shores, it will affect almost every sector of our society, not just health care, but transportation systems, workplaces, schools, public safety and more. It will require a coordinated government-wide response, including federal, state and local governments, and it will require the private sector and all of us as individuals to be ready."⁴ A 1918-style pandemic could be so severe that non-health-related essential services would be impaired by high absenteeism or supply chain disruptions, and health services could be in such short supply that law enforcement protection might be required for them. Countries might seal their borders or take similar measures with impacts on trade and commerce, though WHO does not recommend this, except in some narrow circumstances for pre-pandemic control.

The HHS pandemic plan presumes that the National Response Plan would be activated, if needed, to streamline the federal response to a pandemic. Pandemic flu is different from most other types of emergencies (e.g., bombings or chemical attacks). Since flu is communicable, there is no discrete "scene" to secure, and all states might be affected nearly simultaneously.

⁴ Remarks of HHS Secretary Michael Leavitt on "Avian Flu," National Press Club, Oct. 27, 2005, CQ Transcriptions.

The WHO stresses that the impact of an influenza pandemic would be greatest in developing countries, which lack vaccine production capacity, have limited means to purchase vaccines or antiviral drugs, and have more rudimentary public health and healthcare systems. The WHO notes that certain international efforts that help these nations respond to pandemics could help in other ways, too. For example, boosting demand for seasonal flu vaccine would boost global vaccine capacity. Also, investments in epidemiology and lab capacity for influenza would enhance capacity for disease control generally.

This report discusses pandemic influenza in general, previous pandemics and their global and domestic impacts, and the possible impacts of another pandemic caused by the H5N1 avian flu strain. It also discusses WHO and HHS preparedness plans and their context in broader emergency preparedness efforts. Finally, the report looks at a number of policy issues in pandemic influenza preparedness and response. While reference is made when relevant to global preparedness efforts and to animal health impacts, the focus of this report is U.S. domestic preparedness and response planning, and the projected impacts of an influenza pandemic on American citizens. For more information on seasonal influenza, vaccine development and shortages, see CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by Sarah A. Lister and Erin D. Williams. For more information on agricultural implications of avian flu, see CRS Report RS21747, *Avian Influenza: Agricultural Issues*, by Jim Monke. For more information on the health response to disasters in general, see CRS Report RL33096, *2005 Gulf Coast Hurricanes: The Public Health and Medical Response*, by Sarah A. Lister. This report will be updated to reflect changing circumstances.

Understanding Pandemic Influenza

What Is Pandemic Influenza?

A *pandemic* (from the Greek, for “all of the people”) is an epidemic of human disease occurring over a very wide area, crossing international boundaries and affecting a large number of people. Though it does so with some regularity, influenza is not the only pathogen that causes pandemics. A pandemic of the “Black Death” which affected most of Europe in the 14th century is generally attributed to plague (technically *Yersinia pestis*). Literature offers numerous examples of such episodes of widespread contagion.

Influenza is a virus that causes respiratory disease in humans, with typical symptoms of fever, cough, and muscle aches, and, rarely, pneumonia and death. Though primarily a human pathogen, influenza viruses also circulate and cause illness in swine, horses, mink, seals, and domestic poultry, and may be carried without apparent illness in these species as well as a number of species of waterfowl.⁵ Influenza is highly contagious in humans, spreading through direct contact and aerosol exposure. The virus can also persist for several hours on inanimate objects

⁵ David L. Heymann, *Control of Communicable Diseases Manual*, 18th ed., an official report of the American Public Health Association, 2004.

such as toys or doorknobs. In addition, influenza is infectious before symptoms appear in its victims, which also enhances its spread.⁶

Influenza viruses have a genome composed of eight segments of RNA. In addition to random mutation, flu viruses also undergo change by shuffling or *reassorting* these gene segments among different strains. Flu strains are identified by two important surface antigens (proteins) that are responsible for virulence: hemagglutinin (H) and neuraminidase (N). Fifteen different H antigens and nine different N antigens have been identified in birds and mammals. Not all possible combinations of H and N antigens have been documented, and very few combinations have been shown to cause human illness. The avian flu strain causing great concern at this time is designated as H5N1 for its surface antigens.

New influenza strains typically circle the globe within three to six months of emergence. New strains circulate each year, changing slightly from prior strains (called *genetic drift*) so that healthy adults have partial immunity to new strains. Each year the virus, its genome in constant flux, typically makes healthy people sick, but is generally not deadly. Now and then, often several times in a century, the virus changes enough through reassortment (called *genetic shift*) that there is no partial immunity in the population. This event, an influenza pandemic, results in severe illness and death, even in healthy people. The extent and severity of illness, and the disabling impact on healthy young people, could cause serious disruptions in services and social order.

In this report, unless otherwise noted, the term *pandemic* will be used to refer to pandemic influenza.

Pandemic Phases

According to WHO, the hallmarks of an influenza pandemic are: (1) the emergence of a novel influenza virus strain; (2) the finding that the strain can cause human disease; and (3) sustained person-to-person transmission of the strain. Novel influenza viruses typically acquire these characteristics in phases. **Table 1** shows the phases of an influenza pandemic as described by WHO. In the *interpandemic period*, there is no human circulation of novel viruses. During this period, there is annual circulation of common influenza viruses, which cause outbreaks each winter. In the *pandemic alert period*, a new strain is present, with increasing ability for human-to-human spread. During a *pandemic period* there is sustained human-to-human transmission of the new strain. **Table 1** also shows the public health goals WHO recommends to slow the development and spread of novel virus strains as much as possible. WHO notes that with respect to the H5N1 avian flu currently circulating, “the level of pandemic alert remains unchanged at phase 3: a virus new to humans is causing infections, but does not spread easily from one person to another.”⁷

⁶ CDC, Influenza home page, at [<http://www.cdc.gov/flu/>].

⁷ WHO, “Avian Influenza — New Areas with Infection in Birds — Update 34,” *Disease Outbreak News*, Oct. 13, 2005, at [<http://www.who.int/csr/don/en/>].

Table 1: WHO Pandemic Phases (Revised 2005)

Phase	Description	Overarching public health goals
Interpandemic period		
Phase 1	No new influenza virus strains have been detected in humans. A virus strain that has caused human infection may be present in animals. If so, the risk of human infection is considered to be low.	Strengthen global influenza pandemic preparedness at the global, regional and national levels.
Phase 2	No new influenza virus strains have been detected in humans. However, a circulating animal influenza virus strain poses a substantial risk of human disease.	Minimize the risk of transmission to humans; detect and report such transmission rapidly if it occurs.
Pandemic alert period		
Phase 3	Human infection(s) with a new strain, but no human-to-human spread, or at most rare instances of spread to a close contact.	Ensure rapid characterization of the new virus strain, and early detection, notification and response to additional cases.
Phase 4	Small cluster(s) with limited human-to-human transmission, but spread is highly localized, suggesting that the virus is not well adapted to humans.	Contain the new virus within limited foci or delay spread to gain time to implement preparedness measures, including vaccine development.
Phase 5	Larger cluster(s), but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).	Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.
Pandemic period		
Phase 6	Pandemic: increased and sustained transmission in the general population	Minimize the impact of the pandemic.

Source: WHO Global Influenza Preparedness Plan, 2005, at [http://www.who.int/csr/disease/influenza/pandemic/en/index.html].

Influenza Pandemics in the 20th Century⁸

Historical records suggest that influenza pandemics have occurred periodically for at least four centuries. In the 20th century there were three influenza pandemics, and three “pandemic scares.”

The **1918 Spanish Flu** (H1N1) pandemic is estimated to have killed between 20 and 100 million people worldwide and at least 500,000 in the United States.⁹ Illness and death rates were highest among adults 20-50 years old. HHS notes that “the severity of that virus has not been seen again.” Similarities between the 1918 pandemic and the current H5N1 avian flu situation have the global public health community on edge.

The **1957 Asian Flu** (H2N2) was first identified in Asia in February 1957 and spread to the United States during the summer. Health officials responded quickly and vaccine was available in limited supply by August. This pandemic killed about 69,800 people in the United States.

The **1968 Hong Kong Flu** (H3N2) became widespread in the United States in December of that year. It is estimated that 33,800 people died from this pandemic in the United States, (affecting those over the age of 65 disproportionately), making it the mildest pandemic of the 20th century.

The **1976 Swine Flu Scare**¹⁰ (H1N1) began when a novel virus, identified in New Jersey, was thought to be related to the Spanish flu virus of 1918 and to have pandemic potential. Federal officials mounted a vaccination campaign, and Congress provided liability protection for the manufacturer and federal injury compensation for those harmed by the vaccine. Ultimately, the virus did not spread, but the vaccine was linked with a rare neurological condition that affected more than 500 people and killed 32. The episode damaged confidence in public health officials.

The **1977 Russian Flu Scare** (H1N1) involved a virus strain that had been in circulation prior to 1957. As a result, severe illness was generally limited to those without prior immunity (i.e., children and young adults). The epidemic is not, therefore, considered a true pandemic.

⁸ Unless otherwise noted, information for this section is found in HHS, “Pandemics and Pandemic Scares in the 20th Century,” Feb. 12, 2004, at [http://www.hhs.gov/nvpo/pandemics/flu3.htm#8].

⁹ The U.S. population in 1918 was about one-third its current size, based on decennial census reports of more than 92 million in 1910, and more than 106 million in 1920. The U.S. population is currently almost 300 million. See [http://www.census.gov].

¹⁰ Sources for this section are: Richard E. Neustadt and Harvey V. Fineberg, *The Swine Flu Affair*, a report to the Secretary of Health, Education and Welfare, June, 1978; and HHS Draft Pandemic Influenza Preparedness and Response Plan, Annex 11: “Lessons Learned from 1976 Swine Influenza Program,” Aug. 2004. This incident is discussed further in a later section on vaccine liability and compensation issues.

In **1997**, **H5N1 Avian Flu** emerged in Hong Kong and appeared to have been stamped out by mass culling of poultry. The virus re-emerged in 2003, and global preparedness efforts continue.

In **1999**, **an H9N2 flu strain** was found to have caused human illness in Hong Kong. This strain continues to circulate in birds and remains of concern to public health officials, but has not as yet shown the same lethal potential as the H5N1 strain. In August, 2004, the National Institutes of Health (NIH) awarded a contract to the Chiron corporation to produce up to 40,000 doses of an investigational vaccine against this strain, should it develop the capacity for human-to-human transmission.¹¹

Current Situation

H5N1 Avian Influenza. WHO maintains a Web page with a cumulative count of human H5N1 cases.¹² As of November 1, 2005, WHO reported 122 cases, 62 of whom have died, in four countries: Cambodia, Indonesia, Thailand and Vietnam. The WHO describes pandemic influenza and the current situation with H5N1 as follows:¹³

... outbreaks ... caused by H5N1 are of particular concern because of their association with severe illness and a high case fatality. Of even greater concern is the uniqueness of the present H5N1 situation in Asia. Never before has an avian influenza virus with a documented ability to infect humans caused such widespread outbreaks in birds in so many countries. This unprecedented situation has significantly increased the risk for the emergence of an influenza pandemic.

... The risk (of a pandemic) ... remains so long as H5N1 is present in an animal reservoir, thus allowing continuing opportunities for human exposure and infection. ... Most experts agree that control of the present outbreaks in poultry will take several months or even years. ... The recent detection of highly pathogenic avian influenza in wild birds adds another layer of complexity to control.

... The world may therefore remain on the verge of a pandemic for some time to come. At the same time, the unpredictability of influenza viruses and the speed with which transmissibility can improve means that the time for preparedness planning is right now. Such a task takes on added urgency because of the prospects opened by recent research: good planning and preparedness might mitigate the enormous consequences of a pandemic, and this opportunity must not be missed.

¹¹ NIH, National Institute for Allergy and Infectious Diseases (NIAID), “NIAID Taps Chiron to Develop Vaccine Against H9N2 Avian Influenza,” Aug. 17, 2004, at [<http://www.nih.gov/news/>].

¹² WHO, “Confirmed Human Cases of Avian Influenza A (H5N1),” at [http://www.who.int/csr/disease/avian_influenza/country/en/].

¹³ WHO pandemic plan, p. 3.

The H5N1 strain now circulating has been especially virulent in both human and avian hosts. Laboratory studies suggest that the virus prompts an over-reaction of the inflammatory response in humans, causing rapid and severe damage to the lungs.¹⁴ This primary damage cannot be remedied with antibiotics or antiviral drugs. Victims may require mechanical ventilation, and may succumb despite swift and capable care. In 2004, scientists published the results of research in which they sequenced several genes from the 1918 pandemic strains. These genes, when inserted into flu viruses and used to infect mice, were found to have a similar property.¹⁵ Recently, scientists re-created and published the entire genome of the 1918 strain, reinforcing this finding.¹⁶ This property may explain the high lethality of both the 1918 and H5N1 strains in apparently healthy young people.

The H5N1 avian flu may never slip its moorings as a bird pathogen and become a serious human threat. But that possibility is a worst-case scenario for the world's public health experts. Should H5N1 become a pandemic strain, scientists are concerned that it may retain much of its virulence as it changes to a more transmissible form. In the face of such a deadly pathogen, miracles of modern medicine, unavailable in much of the developing world, may not be of much help in developed countries either. Such a scenario would challenge governments around the globe.

Other Flu Strains with Pandemic Potential. While H5N1 is the most worrisome, it is not the only recent flu strain with pandemic potential. Several novel strains of avian influenza associated with human transmission have resulted in pandemic alert status in the past several years. For example, in 2003 an H7N7 strain affecting commercial poultry flocks in the Netherlands resulted in 89 cases of human illness.¹⁷ Most illnesses were mild, but there was one death. In 2004 in the Canadian province of British Columbia, an H7N3 avian influenza strain in commercial poultry was found to have infected at least two people. While both recovered, WHO issued a pandemic alert for the Canadian outbreak.¹⁸

¹⁴ This phenomenon is often called a "cytokine storm," named after molecules in the immune system that are produced in excess. See C. Y. Cheung, et al., "Induction of Proinflammatory Cytokines in Human Macrophages by Influenza A (H5N1) Viruses: A Mechanism for the Unusual Severity of Human Disease?" *Lancet*, vol. 360, Dec. 7, 2002, pp. 1831-1837; and Y. Guan, et al., "H5N1 Influenza: A Protean Pandemic Threat," *Proceedings of the National Academy of Sciences*, vol. 101(21), May 24, 2004, pp. 8156-8161.

¹⁵ D. Kobasa, et al., "Enhanced Virulence of Influenza A Viruses with the Haemagglutinin of the 1918 Pandemic Virus," *Nature* vol. 431, Oct. 7, 2004, pp. 703-707.

¹⁶ See Jeffery K. Taubenberger, et al., "Characterization of the 1918 Influenza Virus Polymerase Genes," *Nature*, vol. 437, pp. 889-893, Oct. 6, 2005; and Terrence M. Tumpey, et al., "Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus," *Science*, vol. 310, Oct. 2005, pp. 77-80.

¹⁷ Bosman, et al., "Final Analysis of Netherlands Avian Influenza Outbreaks Reveals Much Higher Levels of Transmission to Humans than Previously Thought," *Eurosurveillance Weekly*, vol. 10(1), Jan. 6, 2005, at [http://www.eurosurveillance.org/index-02.asp].

¹⁸ WHO, "Avian Influenza A(H7) Human Infections in Canada," Apr. 5, 2004, at (continued...)

A government worker who became ill while involved in culling flocks of poultry during an outbreak of H7N2 avian flu in Virginia was later shown to have antibodies to that strain, providing suggestive but not conclusive evidence of infection.¹⁹ This and other cases demonstrate a newer understanding of the potential for direct bird-to-human transmission of avian flu viruses, and the fact that while the H5N1 strain is of special concern, public health officials can not neglect other strains. The Centers for Disease Control and Prevention (CDC) has noted several outbreaks of various strains of avian flu in North American poultry flocks in 2003 and 2004, and publishes guidance and recommendations for the protection of persons potentially exposed during such outbreaks.²⁰

Potential Impacts of an Influenza Pandemic

Deaths and Hospitalizations. A WHO influenza expert has said that estimates of the global death toll from a future pandemic are “all over the place.”²¹ The WHO estimates that, in the best case, there would be 2 million deaths worldwide from a possible influenza pandemic, and, in the worst case, more than 50 million.²² In its final pandemic flu plan, HHS estimates that about 209,000 U.S. deaths could result from a moderate pandemic, similar to those in 1957 and 1968, while 1.9 million deaths could result from a severe pandemic like that in 1918.²³ (CDC estimates that on average, about 36,000 die of influenza during an annual flu season.)

Estimates of impacts of a future pandemic are generally based on experience from past pandemics, which varied considerably in their severity. Trust for America’s Health (TFAH), a non-profit public health advocacy group, published a report estimating deaths and hospitalizations in the United States based on mild, moderate and severe pandemic scenarios. The report presents death estimates that

¹⁸ (...continued)

[<http://www.who.int/csr/don/en/>]; and CDC, “Avian Influenza Infections in Humans,” Oct. 17, 2005, at [<http://www.cdc.gov/flu/avian/gen-info/avian-flu-humans.htm>].

¹⁹ A.J. Hostetler and Calvin Trice, “Va. Worker May Have Caught Avian Flu,” *Richmond Times-Dispatch*, Feb. 28, 2004.

²⁰ See CDC website on avian flu outbreaks in North America at [<http://www.cdc.gov/flu/avian/outbreaks/us.htm>].

²¹ Comments of Klaus Stohr, in Keith Bradsher and Lawrence K. Altman, “WHO Official Says Deadly Pandemic Is Likely If the Asian Bird Flu Spreads Among People,” *The New York Times*, Nov. 30, 2004.

²² WHO, “Estimating the Impact of the Next Influenza Pandemic: Enhancing Preparedness,” press release, Dec. 8, 2004, at [http://www.wpro.who.int/media_centre/press_releases/pr_20041209.htm].

²³ HHS “Pandemic Influenza Plan,” Part 1: Strategic Plan, p. 18, Nov. 2005, at [<http://www.pandemicflu.gov>].

range from 180,000 to more than 1 million.²⁴ The report also contains estimated state-by-state health impacts.

Predicted hospitalization rates provide an idea of the potential burden on the U.S. healthcare system, but they are prone to the same degree of uncertainty. In its final pandemic plan, HHS estimates of hospitalizations range from 865,000 to 9.9 million. TFAH estimates that U.S. hospitalizations would range from almost 800,000 to more than 4.7 million, and cites a statistic from the American Hospital Association that in 2003 there were 965,256 staffed hospital beds in registered hospitals. These projected impacts would occur over a compressed time frame of several weeks or a few months, rather than spread over a full year.

Simple extrapolations of health effects from events in 1918 do not account for advances in medical care that have occurred since then. Antibiotics are now available to treat bacterial pneumonia that often results from influenza infection, and sophisticated respiratory care is now available to treat those with severe pneumonia. Experts caution, though, that the H5N1 avian flu virus can cause severe primary damage to the lungs. If this strain were to launch a pandemic and retain this trait, large numbers of victims may require intensive care and ventilatory support, likely exceeding national capacity to provide this level of care. In any event, such specialized care is not available in most developing countries, and access to it is uneven within the United States.

An influenza pandemic of even limited magnitude has the potential to disrupt the normal workings of the healthcare system in a variety of ways. These may include deferral of elective medical procedures; diversion of patients away from overwhelmed hospital emergency departments and tertiary care facilities; protective quarantines of susceptible populations such as residents of long-term care facilities; and hoarding, theft or black-marketeering of scarce resources such as vaccines or antiviral drugs.

Several additional factors complicate the healthcare burden posed by pandemic flu. First, it is thought that a pandemic would spread across the United States in a compressed timeframe similar to seasonal flu, that is, over a six to eight week period. Second, while it is desirable that affected patients be kept in isolation, domestic isolation capacity is limited. Third, the healthcare workforce is likely to be affected by pandemic flu. Even if they are protected directly by limited vaccines or antiviral drugs, their family members may be affected and require additional care at home. Fourth, supplies of healthcare consumables such as gloves, masks and antibiotics would be stressed by a surge in global demand. Even a mild flu pandemic would likely place a significant and near-simultaneous strain on the nation's healthcare system.

²⁴ Trust for America's Health (TFAH), *A Killer Flu?*, June 2005, at [<http://healthyamericans.org/reports/flu/>], applies a set of assumptions and ranges of severity to a CDC-developed computer model, FluAid 2.0, to generate death, hospitalization and outpatient rates based on populations with different age distributions. FluAid 2.0 is available at [<http://www2a.cdc.gov/od/fluaid/>].

Economic Impacts. There are few estimates of the potential economic impact of a flu pandemic. An analysis published by CDC in 1999, based on the relatively mild 1968 pandemic, estimated the cost of a pandemic in the United States at between \$71.3 and \$166.5 billion.²⁵ The study modeled direct healthcare costs, lost productivity for those affected, and lost expected future lifetime earnings for those who died. Loss of life accounted for the majority of economic impact. The model did not include the potential effect of disruptions in commerce. In a recent analysis, the World Bank estimated the overall U.S. economic impacts of a potential pandemic of moderate severity at \$100 to \$200 billion, and global impacts at around \$800 billion, if certain impacts were to last for a full year.²⁶

Several economists studied the economic impacts of Severe Acute Respiratory Syndrome (SARS) in 2003. One analysis showed significant short- and long-term decreases in Gross Domestic Product (GDP) in China and Hong Kong, attributing most of the losses to “the behavior of consumers and investors” rather than to actual medical costs.²⁷ In May 2003, the Conference Board of Canada estimated that the SARS outbreak in Toronto would lower real GDP in Canada by approximately \$1.5 billion, or 0.15 percent, in 2003, projecting that the largest effect would be seen in the travel and tourism industries. Consumer behavior and its economic consequences may be affected by official actions and the response of the news media. Some Canadian officials were critical of a WHO advisory warning against travel to Toronto at the height of the outbreak.²⁸ The World Bank economic analysis of avian flu discusses the likely interplay between government statements and actions, public behavior, and economic effects.

Pandemic Influenza Preparedness and Response

A serious pandemic would trigger the National Response Plan (NRP), developed by the Department of Homeland Security (DHS) as a blueprint for the coordination of federal agencies during an emergency. The NRP, discussed in greater detail in later sections of this report, is an *all-hazards* plan for emergencies ranging from hurricanes to wildfires to terrorist attacks. Described below are a number of strategies and operational plans to assist countries and U.S. federal, state and local agencies in preparing specifically for a flu pandemic. U.S. plans are intended to reflect the time lines, goals and international capabilities described by the WHO in its pandemic plan. In addition, U.S. federal, state and local plans for this

²⁵ M. I. Meltzer et al., “The Economic Impact of Pandemic Influenza in the United States: Priorities for Intervention,” *Emerging Infectious Diseases*, vol. 5(5), Sept.-Oct. 1999.

²⁶ The World Bank Group, “Avian Flu: Economic Losses Could Top US\$800 Billion,” Nov. 8, 2005, at [<http://www.worldbank.org/>].

²⁷ Warwick J. McKibben, “SARS: Estimating the Economic Impacts,” Institute of Medicine, Forum on Microbial Threats, Workshop, “Learning from SARS: Preparing for the Next Disease Outbreak,” Sept. 30, 2003, at [<http://www.iom.edu/event.asp?id=14647>].

²⁸ Alison Appelbe, “Canada Blames Media Hype for SARS Economic Impact,” CNSNews.com, Apr. 25, 2003.

specific threat are intended to be consistent with the all-hazards principles in the NRP.

WHO Global Influenza Preparedness Plan

In order to guide country planning efforts, the WHO released a revised pandemic preparedness plan in early 2005.²⁹ The plan lays out goals and actions to be taken by WHO, as well as recommended actions for individual nations, at each of the pandemic phases (shown in **Table 1**). For each phase, actions are grouped into five categories: (1) planning and coordination; (2) situation monitoring and assessment; (3) prevention and containment; (4) health system response; and (5) communications. In addition, recommended actions for individual nations are grouped according to whether the country is affected or not at a particular phase. For Phase 6 (Pandemic Phase), when it is assumed that all countries will inevitably be affected, there are recommended immediate actions for all countries, and specific actions for those affected, those not yet affected, and those for which the pandemic has subsided, noting that subsequent pandemic waves may follow the first one.

The WHO pandemic plan contains an annex of recommendations to nations for “nonpharmaceutical public health interventions,” actions such as isolation, quarantine and travel restrictions. The annex stresses the use of voluntary rather than compulsory measures, noting the lack of demonstrated utility of certain practices, or that enforcement is considered impractical for others. The annex also notes that certain practices used to control SARS, such as temperature screening at airports, are not necessarily recommended for control of pandemic influenza, depending on pandemic phase. (Because influenza virus is more transmissible than SARS, some SARS control measures are not considered effective for flu.) The plan and annex also stress avoiding stigmatization of persons affected by pandemic influenza or its control measures.

HHS Draft Pandemic Plan

In August 2004, HHS released a draft pandemic influenza preparedness and response plan.³⁰ The draft plan articulated steps to be taken by HHS agencies and offices, and by state and local public health authorities, in preparing for and responding to a pandemic. Specific activities discussed included surveillance, vaccine development and use, antiviral drug use, and communications. The draft plan was criticized by some as being vague, and for delegating certain critical activities — such as designating priority groups for rationing of vaccine and antiviral drugs — to states.³¹

²⁹ WHO pandemic plan.

³⁰ HHS, *Draft Pandemic Influenza Preparedness and Response Plan*, Aug. 26, 2004, at [<http://www.hhs.gov/nvpo/pandemicplan/index.html>].

³¹ See, for example, Association of State and Territorial Health Officials (ASTHO), comments on the HHS National Pandemic Influenza Preparedness and Response Plan, Oct. 25, 2004, at [<http://www.astho.org/pubs/ASTHOCCommentsOnPandemicFluPlan.pdf>],
(continued...)

National Strategy for Pandemic Influenza

On November 1, 2005, the administration released a “National Strategy for Pandemic Influenza,” on a central website containing interagency pandemic preparedness and response information.³² The strategy lays out three goals: (1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. In order to meet those goals, the strategy lays out three “pillars” of implementation activities:

- Preparedness and Communication: Activities that should be undertaken before a pandemic to ensure preparedness, and the communication of roles and responsibilities to all levels of government, segments of society and individuals.
- Surveillance and Detection: Domestic and international systems that provide continuous “situational awareness,” to ensure the earliest warning possible to protect the population.
- Response and Containment: Actions to limit the spread of the outbreak and to mitigate the health, social and economic impacts of a pandemic.

Finally, roles and responsibilities are laid out for the federal government, state and local governments, the private sector, individuals and families, and international partners.

In announcing the strategic plan, President Bush sent a budget request to Congress seeking \$7.1 billion in emergency spending for the departments of HHS, Agriculture, Defense, Homeland Security, Interior, State and Veterans Affairs.³³ The proposed funding would: (1) support enhanced domestic and international planning and surveillance activities (\$259 million requested); (2) purchase stockpiles of vaccines and antiviral drugs, and accelerate the development of new vaccine technologies (\$6.242 billion requested); and (3) aid in federal, state and local preparedness efforts (\$644 million requested.)

³¹ (...continued)

hereafter cited as ASTHO comments regarding HHS plan. Additional comments are at HHS, “Public Comments to the Pandemic Influenza Preparedness and Response Plan,” at [<http://www.hhs.gov/nvpo/pandemicplan/comments062005.html>].

³² White House Homeland Security Council, *National Strategy for Pandemic Influenza*, Nov. 1, 2005, at [<http://www.pandemicflu.gov/>].

³³ See White House Office of Management and Budget, Estimate No. 15, Nov. 1, 2005, at [http://www.whitehouse.gov/omb/budget/amendments/supplemental_11_01_05.pdf].

HHS Final Pandemic Plan

HHS released its final pandemic influenza plan on November 2, 2005.³⁴ The final plan builds on elements in the draft plan, and has three parts: (1) a Strategic Plan, which outlines key planning assumptions and HHS agency roles; (2) a Public Health Guidance for State and Local Partners, which lays out activities on such matters as surveillance, laboratory testing, and quarantine at the borders; and (3) a part currently under development, to consist of detailed operational plans for HHS agencies involved in pandemic response. According to the plan, the HHS Secretary would direct, and the Assistant Secretary for Public Health Emergency Preparedness would coordinate, all HHS pandemic response activities.

The final plan will be critiqued over time. Some concerns with the draft plan have been addressed, such as the designation of priority groups to receive limited vaccine and antiviral drugs.³⁵ Other elements of the final plan received immediate criticism. For example, the section on healthcare planning focuses on individual healthcare facilities and refers to plans for surge capacity. Some experts have commented that there is little surge capacity in the healthcare sector under normal circumstances, and that officials might have to resort to the use of alternate facilities (e.g., convention centers) to care for large numbers of flu patients. The HHS final plan does not address that contingency.

Department of Defense Planning and Activities

Shortly after the release of the HHS draft pandemic plan in August 2004, the Assistant Secretary of Defense for Health Affairs released the Department of Defense (DOD) “Pandemic Influenza Preparation and Response Planning Guidance.”³⁶ The DOD guidance follows many of the assumptions used in the civilian plan, modifying them to protect a highly mobile military force during wartime. Frequent mention is made of the extremely high mortality suffered by U.S. troops during World War I as a result of the 1918 pandemic. The guidance notes that 43,000 uniformed soldiers, more than one third of all U.S. military casualties in the war, died of pandemic influenza, most of them during one 10-week period in 1918.

The DOD guidance notes that the military will use the same vaccine formulation as that developed for civilian use, though DOD will be responsible for securing its own supplies of vaccine and antiviral drugs. Priority for countermeasures in limited supply would be given to forward-deployed troops. The guidance does not set out strict tiers of priority recipients (nor had the HHS draft plan). The guidance discusses

³⁴ HHS, “HHS Pandemic Influenza Plan,” Nov. 2005, at [<http://www.pandemicflu.gov>].

³⁵ Though the plan includes specific tiers of priority groups, and estimates of the number of people in each group, the designations may be modified in light of the actual behavior of a pandemic flu strain. For example, if atypical groups such as healthy young people were found to be at increased risk of severe illness, the tiers could be adjusted accordingly.

³⁶ Department of Defense, “Pandemic Influenza Preparation and Response Planning Guidance,” Sept. 15, 2004, at [<http://www.geis.fhp.osd.mil/GEIS/SurveillanceActivities/Influenza/fluPolicy.asp>].

the limited utility of individual control measures such as isolation and quarantine, and suggests that larger-scale adjustments (such as extending the tour of ships at sea) could slow disease transmission. The guidance also mentions the consideration of coalition forces from other nations, and the possibility that countermeasures such as vaccine and antiviral drugs may be provided to them under certain conditions.

On November 7, 2005, DOD's Deployment Health Support Directorate announced a new website to provide service members with information on avian and pandemic influenza.³⁷ The Department has not publicly released a revised or final version of its 2004 pandemic flu guidance.

DOD maintains the Global Emerging Infectious Diseases Surveillance program (GEIS), which has long been a source of year-round global influenza surveillance data.³⁸ The guidance states that DOD will provide information gleaned from this system, as well as its global laboratory network, to WHO and CDC officials tracking pre-pandemic and pandemic flu virus activity.

Department of Veterans Affairs Planning and Activities

The Department of Veterans Affairs (VA) notes that it is involved in coordinated pandemic influenza planning, though limited information is publicly available.³⁹ Pandemic planning activities are to be expansions of the department's seasonal flu control activities, which include vaccination programs and surveillance. To date, the VA has stockpiled 550,000 treatment courses of the antiviral drug, Tamiflu.

State Pandemic Preparedness Plans

All states were required to have submitted plans for pandemic flu preparedness to HHS (through CDC) by July 2005, as a condition of receipt of public health preparedness funding for FY2005.⁴⁰ CDC reports that it has received plans from all states.⁴¹ As of October 2005, 32 states had posted draft or final plans on a public

³⁷ See [http://deploymentlink.osd.mil/medical/medical_issues/immun/avian_flu.shtml].

³⁸ See DOD Global Emerging Infections System at [<http://www.geis.fhp.osd.mil/aboutGEIS.asp>].

³⁹ VA, "Pandemic Flu Planning and the Department of Veterans Affairs: Overview," Oct., 2005, at [http://vhaidsinfo.cio.med.va.gov/flu/documents/Avian_Flu_Public_final.pdf], found on the VA influenza page at [<http://vhaidsinfo.cio.med.va.gov/flu/pandemicflu.htm>].

⁴⁰ According to cooperative agreement guidance for FY2004 funds, states were required to submit pandemic plans along with their applications for FY2005 funds. See CDC, "Cooperative Agreement Guidance for Public Health Emergency Preparedness," Program Announcement AA154, May 13, 2005, at [<http://www.bt.cdc.gov/planning/guidance05/>].

⁴¹ Communication with Michael Craig, CDC Policy Analyst, Nov. 1, 2005. According to the Public Health Service Act, the District of Columbia is considered a state for purposes of preparedness funding and requirements.

website.⁴² Of these, 15 state plans were dated within 2005, and the remainder earlier. Since states were required to submit their plans before a final federal plan was available, some states may subsequently update their plans to reflect new planning information.

Guidance provided by CDC directed states to incorporate the following elements in their pandemic influenza preparedness plans:

- Assemble an executive planning committee;
- Identify and meet with partners and stakeholders;
- Establish command, control and management procedures;
- Establish procedures for essential functions: surveillance and laboratory testing; delivery of vaccines and antiviral drugs; emergency health and medical response; maintenance of essential services; and communications.⁴³

The Association of State and Territorial Health Officials (ASTHO) also produced a guidance document to assist its members in developing plans.⁴⁴ In addition to activities described in the CDC guidance, the ASTHO document contains a checklist of additional tasks in pandemic planning, including:

- A review of state policies and authorities regarding public health and medical issues such as: quarantine; mandatory vaccination; the closure of schools and businesses; volunteer licensure, liability and compensation; and the use of temporary medical facilities.
- A review of state authorities and individuals responsible for issues outside the public health and medical sphere, such as: establishing incident command; coordinating activities across state agencies, and with health agencies in adjacent states; and use of law enforcement and National Guard support.

Issues in Pandemic Influenza Planning

Could an Influenza Pandemic Be Stopped?

Public health experts note that vaccine, the primary measure for influenza prevention, will be available in very limited supply at the start of any pandemic, and

⁴² Council of State and Territorial Epidemiologists, state pandemic influenza plans, at [<http://www.cste.org/specialprojects/Influenzaplans/StateMap.asp>]. CDC is not involved in maintaining this site and cannot confirm whether plans available here are the same versions as those submitted to the agency.

⁴³ CDC, “Pandemic Influenza: A Planning Guide for State and Local Officials (Draft 2.1),” undated document.

⁴⁴ ASTHO, “Nature’s Terrorist Attack: Pandemic Influenza, Preparedness Planning for State Health Officials,” Nov. 2002, at [<http://www.astho.org/pubs/Pandemic%20Influenza.pdf>].

is unlikely ever to be available to everyone. Antiviral drugs are also likely to be available in a limited supply. For both, there is limited global surge capacity for production during a pandemic. Conventional wisdom once held that there was an inevitability to the global wave of disease that a pandemic would bring, but lately this notion has been challenged. WHO and many national experts believe that scientific advances in studying and detecting flu viruses may make it possible to detect the spread of the virus early and rein in localized clusters of infection. While not suggesting that a pandemic could necessarily be averted, they posit that if progression were slowed enough, a vaccine could be available by the time worldwide infection ensued. While there still might not be enough vaccine for everyone, if countries had at least enough for essential personnel, it would soften the impact somewhat.

Realizing this hope rests on two conditions: first, exceptional “pandemic intelligence” in countries at the epicenter of a developing pandemic; and second, priority use of control measures in these epicenter countries. In hopes of having the best possible information in real time, WHO, CDC, and health officials from many other nations are building epidemiology and lab capacity in Southeast Asian countries affected by H5N1 avian flu, when those countries have requested assistance. This aid is layered onto an uneven patchwork of existing capacities. In supplemental appropriations for FY2005 (P.L. 109-13), Congress provided \$15 million (through the foreign assistance account at the State Department) to supplement CDC’s existing activities to expand epidemiology and laboratory capacity in that region.

The second requirement for successful pre-pandemic containment, namely priority use of control measures in affected countries, is politically difficult. It would require that countries contribute vaccine and antiviral drugs to a global stockpile to be used in epicenter countries to slow a pandemic. Costs notwithstanding, given that countries would face severe shortages of these precious assets if a pandemic reaches them, would they share their national stockpiles with other countries? Many U.S. analysts believe that doing so is not merely altruistic. They argue that providing antiviral drugs to an affected country in the early going would save American lives in the long run. While plausible, this thesis is untested, and WHO has had limited success to date in getting nations to commit assets to the global stockpile.

Who's in Charge?

The National Response Plan (NRP) published by DHS, is a blueprint for the coordinated efforts of federal agencies during disasters.⁴⁵ In the event of a significant influenza pandemic, the NRP may be activated to coordinate federal agency activities. Responsibilities for specified activities (e.g., transportation, energy, and public works) are set out in 15 *Emergency Support Functions* (ESF). When asked who would be in the lead for the federal response during a pandemic, Dr. Jeffrey Runge, Chief Medical Officer for DHS, replied:

⁴⁵ See DHS, *National Response Plan*, Dec. 2004, hereafter called the NRP, at [<http://www.dhs.gov/dhspublic/display?theme=14&content=4264>], and CRS Report RL32803, *The National Preparedness System: Issues in the 109th Congress*, by Keith Bea.

When critical infrastructures are threatened, the secretary of DHS is responsible for the preservation of critical infrastructures. HHS will continue to have the lead in prevention, containment and treatment of avian flu. But if the government surges, and if the ESFs (Emergency Support Functions) stand up and so forth, the secretary of DHS will be responsible for each of those emergency support functions discharging their duty. One of the duties of HHS is containment, prevention and treatment of avian flu.⁴⁶

When the NRP is activated, the Secretary of Homeland Security serves as the overall lead for a coordinated federal response, while the Secretary of HHS serves as the lead for ESF#8, Public Health and Medical Services.⁴⁷ While public health and medical activities may comprise the bulk of the federal response to a pandemic, other ESF authorities may be involved to sustain infrastructure affected by absenteeism or supply chain disruptions, requiring the coordination of other federal departments.

Overarching federal leadership in DHS may be called upon to address problems such as the prioritization of federal non-medical resources, if these resources were exhausted by demands from many states simultaneously. State disaster planning commonly relies on state-to-state mutual aid, in addition to federal assistance.⁴⁸ In a severe pandemic, assistance from other states may be limited, and federal assistance may be thinly stretched.

The NRP is intended to identify federal roles and leadership for a *response* to an emergency, and resolve coordination difficulties. Experience gained from the implementation of the NRP after Hurricane Katrina indicates that there may be a gap in leadership for *preparedness*.

WHO urges that countries plan for a pandemic as a multi-sector threat, not merely a health challenge. Planning in HHS and state health agencies is ongoing, but some assert that a clear point of leadership is needed at the federal level to engage state, local and municipal officials in multi-sector planning. The National Strategy notes that lead departments have been identified for the medical response (HHS), veterinary response (Department of Agriculture), international activities (Department of State) and overall domestic incident management (DHS). Each of these departments would serve as the federal liaison to assist its respective sectors in planning. In addition, DHS is responsible for coordinating the preparedness of privately owned critical infrastructures such as banking or telecommunications.

However, federal relationships that support state and local jurisdictions traditionally operate sector-by-sector (e.g., HHS with health services, and the Department of Transportation with transit agencies). At this time, a mayor would

⁴⁶ Testimony of Dr. Jeffrey Runge, Chief Medical Officer, DHS, before the House Homeland Security Committee, Subcommittee on Management, Integration, and Oversight, hearing on “Role of the Chief Medical Officer,” Oct. 27, 2005, 109th Congress, 1st Sess.

⁴⁷ For more information on ESF#8, see CRS Report RL33096, *2005 Gulf Coast Hurricanes: The Public Health and Medical Response*, by Sarah A. Lister.

⁴⁸ See CRS Report RS21227, *The Emergency Management Assistance Compact (EMAC): An Overview*, by Keith Bea.

have difficulty identifying one point of contact concerning the spectrum of planning activities that would be needed to keep water running, lights on, food stocked, and gasoline flowing during a serious flu pandemic. Further, while pandemic influenza scenarios have been used to exercise specific elements of response, such as distribution of stockpiled medications, there has been no large-scale exercise to study a coordinated, multi-sector response to this potential nationwide threat.⁴⁹

Emergency Declarations and Federal Assistance

In the United States, public health authority rests principally with the states as an exercise of their *police powers*.⁵⁰ States play a leading role in preparing for and responding to public health threats, with HHS (primarily CDC) providing support through funding, training, technical assistance, advanced laboratory support, data analysis and other activities. The Public Health Service Act grants the Secretary of HHS the authority to declare a situation a public health emergency, which triggers an expansion of certain federal authorities.⁵¹ Though states already have considerable power in responding to public health events, most can also declare public health emergencies and expand their powers further. In an influenza pandemic, response measures such as quarantine or prohibitions against administration of vaccine to non-priority individuals would likely be carried out, at least initially, by state rather than federal authorities.⁵²

An influenza pandemic may disrupt services beyond the health sector. A multi-sector federal response to a pandemic could be directed by provisions in the NRP. Both the HHS pandemic plan and the DOD pandemic guidance are written with the premise that the NRP would be triggered by a severe influenza pandemic, thereby guiding a coordinated federal response to problems within the health sector and other sectors that may be affected, through routine (non-emergency) federal assistance mechanisms. The Biological Incident Annex in the NRP notes that “Actions described in this annex take place with or without a Presidential Stafford Act declaration or a public health emergency declaration by the Secretary of (HHS).”⁵³ While the annex addresses intentional bioterrorism events, it also addresses naturally occurring biological threats such as pandemic influenza.

⁴⁹ The administration’s emergency supplemental budget request for pandemic flu, submitted to Congress on Nov. 1, 2005, would provide \$47.3 million to DHS, for several activities including the development of pandemic response exercises.

⁵⁰ The term *police powers* derives from the 10th Amendment to the Constitution, which reserves to the states those rights and powers not delegated to the United States. Historically these have been interpreted to include authority over the welfare, safety, health, and morals of the public.

⁵¹ A public health emergency was declared in several states affected by Hurricane Katrina. See CRS Report RL33096, *2005 Gulf Coast Hurricanes: The Public Health and Medical Response*, by Sarah A. Lister.

⁵² For a discussion of the exercise of federal and state authorities in response to the recent shortage of influenza vaccine, see CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by Sarah A. Lister and Erin D. Williams.

⁵³ NRP, Biological Incident Annex, p. BIO-1.

States may require additional federal assistance to maintain essential services during an influenza pandemic. Typically, such assistance is triggered by Presidential emergency or disaster declarations under the Stafford Act.⁵⁴ Disaster assistance authorized by the Stafford Act includes the provision of emergency funds and supplies to stricken households as well as aid in clearing and rebuilding damaged infrastructure. While a virus would not cause such damage directly, certain sectors may nonetheless be affected as a result of widespread absenteeism or supply chain disruptions. For example, water treatment facilities may be damaged, or may have to be shut down, if they are not adequately maintained, or if replacement parts are unavailable. Sectors which depend heavily on continuous computer support (e.g., banking) may be disrupted by absenteeism.

Some may question whether the Stafford Act is an appropriate legislative base for action in the event of a flu pandemic. In a recent terrorism preparedness exercise, TOPOFF III, concerns were raised that because the Stafford Act explicitly defines a “major disaster” as a *natural* catastrophe, states facing a terrorism incident would not be eligible for the full range of federal disaster assistance authorized by the act.⁵⁵ Such concerns may be met, however, with the recognition that the definition of the term “emergency” in the statute provides greater discretion to the President in issuing an emergency declaration. However, pursuant to the Stafford Act, considerably less financial assistance may be provided under an emergency declaration, compared to that authorized under a major disaster declaration.

An influenza pandemic may pose a challenge in national disaster response that is without recent precedent. A pandemic could affect all or almost all areas of the United States with multi-sector impacts within a six to eight week period, involving the entire country nearly at once. A severe pandemic could cause “extraordinary levels of mass casualties” and substantial disruptions in services, and thereby meet the definition of a *Catastrophic Incident* according to the NRP.⁵⁶ Questions might be raised about the adequacy of the Catastrophic Incident Annex in the NRP. The Annex was not activated during the response to Hurricane Katrina.⁵⁷ DHS officials have said that the Annex and related planning documents are not yet complete.⁵⁸

Limited Surveillance and Detection Capability

The CDC coordinates domestic surveillance for seasonal flu. Monitoring for pandemic flu is integrated into these existing systems. Key challenges in the rapid detection of novel flu viruses are the vagueness of flu symptoms, which can be seen

⁵⁴ See CRS Report RL33053, *Federal Stafford Act Disaster Assistance: Presidential Declarations, Eligible Activities, and Funding*, by Keith Bea.

⁵⁵ See comments of New Jersey Governor Richard Codey in Rick Hepp, “Jersey Officials Identify Holes in Response Plan,” *The Star-Ledger*, Apr. 9, 2005.

⁵⁶ NRP, Catastrophic Incident Annex, p. CAT-1.

⁵⁷ Chris Strohm, “DHS Failed to Use Catastrophe Response Plan in Katrina’s Wake,” *GovExec.com*, Oct. 18, 2005.

⁵⁸ Zack Phillips, “DHS Catastrophe Plan Incomplete, Congressmen Say,” *CQ Homeland Security*, Nov. 1, 2005.

with many other diseases, and the difficulty in distinguishing specific strains of interest from the background of other flu strains commonly in circulation.

The routine CDC system for domestic flu surveillance has seven reporting components: (1) more than 120 laboratories; (2) more than 1,000 sentinel healthcare providers; (3) death records from 122 cities; (4) reports from health departments in the states, territories, New York City and the District of Columbia; (5) influenza-associated deaths in children; (6) Emerging Infections Program sites in 10 states; and (7) laboratory-confirmed hospitalizations of young children in three sentinel counties.⁵⁹ Reporting to these systems by state and local health departments and healthcare providers is voluntary. Information is gathered and analyzed weekly during the winter flu season. The final HHS pandemic plan proposes that BioSense, a new system to gather, in real time, information such as emergency department admissions, be incorporated along with other flu detection systems.

Through the Health Alert Network, CDC has issued recommendations to public health and medical professionals, addressing domestic surveillance and laboratory investigation of possible cases of avian or pandemic influenza.⁶⁰ CDC recommends that health professionals use screening tests for influenza on individuals who have a history of recent travel to an affected region and exhibit symptoms of severe respiratory disease. Specimens that test positive on screening for influenza should be followed up with samples sent to CDC to determine which flu strain is involved. CDC is working with states to develop state-based lab capability for testing flu viruses for the H5 antigen, but this capability is not yet in place.⁶¹

Isolation and Quarantine

Isolation and quarantine have been used for hundreds of years to prevent the spread of communicable diseases. Both methods restrict the movement of those affected, but they differ depending on whether an individual has been exposed to a disease (*quarantine*), or is actually infected (*isolation*). Persons in isolation may be significantly ill, so isolation often occurs in a healthcare setting. Persons under quarantine are, by definition, not ill from the disease in question, though they may have other health conditions that complicate the quarantine process.

In the United States, quarantine authority is generally based in state rather than federal law.⁶² The federal government has the responsibility to prevent the

⁵⁹ CDC, “Overview of Influenza Surveillance in the United States,” Feb. 2, 2005, at [<http://www.cdc.gov/flu/weekly/pdf/flu-surveillance-overview.pdf>].

⁶⁰ CDC, “Health Updates on Avian Influenza,” Feb. 4, 2005 and previous, at [<http://www.cdc.gov/flu/avian/professional/updates.htm>].

⁶¹ CDC, “Key Facts About Avian Influenza (Bird Flu) and Avian Influenza A (H5N1) Virus,” Oct. 25, 2005, at [<http://www.cdc.gov/flu/avian/gen-info/facts.htm>]. If a state were to identify H5 strains of influenza, the specimens would then be referred to CDC to determine if they were H5N1.

⁶² See CRS Report RL31333, *Federal and State Isolation and Quarantine Authority*, by (continued...)

introduction, transmission, and spread of communicable diseases from foreign countries, and the authority to impose quarantine on incoming travelers suspected to be infected with or exposed to certain diseases on a list of quarantinable communicable diseases. Diseases are listed by an executive order of the President, in consultation with the Secretary of HHS. On April 1, 2005, President Bush added to the list “influenza caused by novel or re-emergent influenza viruses that are causing, or have the potential to cause, a pandemic.”⁶³ Federal quarantine is carried out by CDC’s Division of Global Migration and Quarantine, which operates quarantine stations at major ports, and also works closely with states to carry out quarantine activities.⁶⁴ CDC has noted that having pandemic influenza on the list assures the agency of this option for disease control, should it be felt to be worthwhile.

On October 4, 2005, in response to a question at a press conference, President Bush suggested the use of the military to enforce quarantines during a flu pandemic.⁶⁵ The comment prompted responses on two issues: the role of the military in domestic disasters, and the role of quarantine in controlling pandemic flu.

Following the terror attacks of 2001, in October of 2002, DOD activated a new combatant command, Northern Command or NORTHCOM, to, among other functions, provide military assistance to civil authorities in response to terrorist attacks.⁶⁶ The NRP also articulates this role for the military in response to terrorist attacks, major disasters, and other emergencies.⁶⁷ There has, however, long been a prohibition against the use of federal military personnel for domestic law enforcement, except in extraordinary circumstances.⁶⁸ There are no instances in the 20th century in which federal troops were used to enforce a domestic quarantine for any disease, though there are earlier examples.⁶⁹ On October 13, 2005, Assistant

⁶² (...continued)

Angie A. Welborn.

⁶³ See Executive Order: “Amendment to E.O. 13295 Relating to Certain Influenza Viruses and Quarantinable Communicable Diseases,” Apr. 1, 2005, at [<http://www.whitehouse.gov/news/releases/2005/04/20050401-6.html>]; and CDC, “Questions and Answers on the Executive Order Adding Potentially Pandemic Influenza Viruses to the List of Quarantinable Diseases,” Apr. 11, 2005, at [http://www.cdc.gov/ncidod/dq/qa_influenza_amendment_to_eo_13295.htm].

⁶⁴ See CDC Division of Global Migration and Quarantine home page at [<http://www.cdc.gov/ncidod/dq/index.htm>].

⁶⁵ Press conference with President George Bush, Federal News Service transcript, Oct. 4, 2005.

⁶⁶ CRS Report RL31615, *Homeland Security: The Department of Defense’s Role*, by Steve Bowman.

⁶⁷ NRP, “Defense Support of Civil Authorities,” pp. 41 ff.

⁶⁸ CRS Report RS22266, *The Use of Federal Troops for Disaster Assistance: Legal Issues*, by Jennifer K. Elsea.

⁶⁹ Information provided by Dr. Dale Smith, medical historian, Uniformed Services
(continued...)

Secretary of Defense for Homeland Defense Paul McHale commented that the threshold for use of troops during a domestic disaster would be high, but that "... an outbreak of avian flu could be so severe that active-duty forces might need to help the National Guard enforce quarantines," and that "... Congress and federal agencies must establish clear guidelines on what would trigger a broad U.S. military response to restore law and order."⁷⁰

While isolation and quarantine were crucial in the worldwide response to SARS, these methods are less likely to be successful in controlling influenza. Influenza is more highly contagious than SARS, has a shorter incubation period, and is often contagious in the absence of symptoms or before symptoms appear, making it difficult to identify persons who should be quarantined.⁷¹ Public health officials have suggested the use of quarantines in certain circumstances (e.g., incoming passenger flights) to delay the emergence of pandemic influenza in an area, but have generally steered away from suggesting the more traditional use of quarantine of individuals as a containment measure for pandemic flu, recommending instead the use of voluntary, population-based approaches (e.g., cancelling sporting events).⁷²

Rationing Scarce Resources

The WHO recommends that countries identify priority groups for vaccination and antiviral drugs (as these measures become available) and that countries make these decisions before a pandemic occurs. The National Vaccine Advisory Committee (NVAC, which reports to the director of the National Vaccine Program in HHS) and the Advisory Committee on Immunization Practices (ACIP, which reports to the HHS Secretary and CDC) met in joint session in July 2005 to report to HHS Secretary Leavitt their recommendations for prioritizing vaccine and antiviral drugs for the U.S. civilian population during a pandemic.⁷³ The two committees concurred on each group's unanimous recommendations for prioritizing pandemic flu vaccine. Their recommendations were incorporated into the HHS final pandemic plan, and are displayed in **Table 2**.

Healthcare workers with direct patient contact and those involved in making the vaccine were given top priority by the committees. Next were those at highest risk

⁶⁹ (...continued)

University of the Health Sciences, Bethesda, Maryland, Oct. 13, 2005.

⁷⁰ Mark Mazzetti, "Military Sees Limits to Role in U.S. Disasters; A Defense official says 'catastrophic' events, including a pandemic, would be the threshold," Oct. 13, 2005.

⁷¹ Christophe Fraser, et al., "Factors that Make an Infectious Disease Outbreak Controllable," *Proceedings of the National Academy of Sciences*, vol. 101(16), pp. 6146-6151, Apr. 20, 2004, at [<http://www.pnas.org/cgi/reprint/101/16/6146>].

⁷² See, for example, Brian Friel, "Law In The Time Of Cholera," *National Journal*, Oct. 21, 2005.

⁷³ Charles M. Helms, NVAC Chairman, letter to HHS Acting Assistant Secretary for Health Cristina V. Beato, on NVAC recommendations regarding priority use of vaccine and antiviral drugs during an influenza pandemic, Aug. 10, 2005, at [<http://www.hhs.gov/nvpo/nvac/documents/chairletter.pdf>].

of serious complications from flu. During seasonal flu, and during the 1957 and 1968 pandemics, those at highest risk were the very old, the very young, and individuals with certain serious chronic diseases. The committees noted that during a pandemic other groups may be shown to be at higher risk, and that tiers could be redefined according to the specific epidemiologic findings. For example, during the 1918 pandemic, healthy young people were found to be at increased risk of death when they became infected. According to the committees' estimates, more than 60% of the U.S. population would not fall into any of the designated priority groups.

**Table 2. NVAC and ACIP Recommendations
for Pandemic Vaccine Priority Groups**
(persons in thousands)

Group and Tier	Group total	Cumulative total
1A. Healthcare workers with direct patient contact	9,000	9,000
Vaccine and antivirals manufacturing personnel	40	9,040
1B. Highest risk of serious flu complications	25,840	34,880
1C. Pregnant women, immunocompromised individuals, and household contacts of infants	10,700	45,580
1D. Key government leaders and responders	151	45,731
2A. Rest of high risk individuals	59,100	104,831
2B. Most critical infrastructure and public health emergency responders	8,500	113,331
3. Other key government health decision makers, mortuary services personnel	500	113,831
4. Healthy 2-64 yr. olds not in other groups	179,260	293,091

While the proposed scheme emphasizes the protection of those who are most vulnerable to severe complications from flu, it does not necessarily reflect the goal of saving the most lives. To achieve the latter when resources are scarce, treatment would be given to those most likely to have better outcomes as a result. Conversely, treatment could be withheld from those who are unlikely to benefit, so that others may. These are ethically complex decisions with which the civilian medical community has little experience. Also, in this case, science does not provide ready answers.

In 2005, both the peer-reviewed medical literature and the popular press have carried numerous reports about the possibility of decreasing societal flu transmission by vaccinating children, and of possibly limited effectiveness of flu vaccine in the frail or institutionalized elderly. The science leaves policymakers uncertain on both

counts. Available studies are limited and conflicting, often with non-comparable designs, and they are observational rather than controlled. (Controlled studies of such questions could violate ethical standards and guidelines for the protection of study subjects.) Lacking better evidence to guide decisions, some are left with a sense of unease as they try to envision which groups should receive flu vaccine during a pandemic.⁷⁴

Influenza Vaccine Supply and Use

Limited Vaccine Production Capacity. Vaccination is considered the best preventive measure for influenza. Flu vaccine is currently produced in chicken eggs in a time-consuming process with a six-month lead time.⁷⁵ Since a vaccine could not be mass produced against a pandemic flu strain until that strain emerged, planning assumes that flu vaccine will not be available for initial global pandemic control.⁷⁶ Nonetheless, health officials are working to increase the speed of flu vaccine production, to increase global flu vaccine production capacity, and to ready candidate vaccines for H5N1 and H9N2 avian flu, in the event that either of these were to become a pandemic strain.

Currently, there is worldwide capacity to produce at most 300 million doses of *trivalent* flu vaccine, the annual vaccine that contains three different strains of influenza.⁷⁷ Only one (sanofi pasteur⁷⁸) of nine manufacturers of injectable flu vaccine is located in the United States. Capacity for this producer is expected to be approximately 60 million trivalent doses for 2005-2006.

Though production capacity can, in theory, be tripled by converting to single-strain production for a pandemic vaccine, two doses (vs. the single dose given each year) may be required to afford protection, because there is no prior immunity to be “boosted.” Furthermore, in initial trials of an H5N1 prototype vaccine, immunity was produced only by very high doses of viral antigen, which means that more capacity would be needed to make a given number of doses.

The President’s supplemental budget request for pandemic flu says, “The centerpiece of the (HHS) proposal is to increase vaccine manufacturing capacity to allow for the production of pandemic influenza vaccine for the entire nation within

⁷⁴ For more information on rationing of scarce health resources, see the section on Strategies for Rationing in CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by Sarah A. Lister and Erin D. Williams.

⁷⁵ Further discussion of flu vaccine production is available in CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by Sarah A. Lister and Erin D. Williams.

⁷⁶ Recently, WHO and some countries have considered stockpiling small amounts of a prototype H5N1 vaccine. There is concern that if H5N1 became a pandemic strain, it might change sufficiently that “pre-pandemic” vaccine may not protect.

⁷⁷ David S. Fedson, “Preparing for Pandemic Vaccination: An International Policy Agenda for Vaccine Development,” *Journal of Public Health Policy*, Vol. 26, pp. 4-29, 2005, (hereafter called Fedson article), at [<http://www.palgrave-journals.com/jphp/fedson.pdf>].

⁷⁸ The company does not use capital letters in its name.

a six-month period... .”⁷⁹ The request mentions the possible use of the funds for renovation and construction, and for research, but lacks additional detail regarding how federal funds might be used to build private capacity for this crucial but rarely needed intervention. On November 2, 2005, HHS Secretary Leavitt testified that HHS would pursue a multi-pronged strategy to increase domestic production capacity and stockpile expansion, with goals to be achieved in phases between 2008 and 2013. The stated goals include (1) licensing additional domestic manufacturers of injectable flu vaccine; (2) transitioning from egg-based to cell-based production; and (3) research in new vaccine technologies.⁸⁰

Leavitt stated that HHS would support research on the use of *adjuvants* (i.e., vaccine additives that boost immunity), lowering the needed dose of virus, and thereby stretching available capacity. One expert has commented that if the United States had prioritized the use of adjuvants sooner, it could be farther along in establishing not only adequate domestic capacity for pandemic vaccine production, but also added capacity to assist other nations that lack capacity of their own.⁸¹ He proposed that under optimal conditions, if all the world’s vaccine companies were to use a certain adjuvant to produce pandemic flu vaccines, that within six months’ time there could be enough vaccine for 3.6 billion people, about half the world’s population.

The use of adjuvants in flu vaccine would add additional scientific, technical and regulatory obstacles, especially new safety concerns. For this reason, the United States has developed prototype H5N1 vaccines using methods similar to those used for seasonal vaccine production, an approach that would optimize the chances for success in the near-term, in the event that a pandemic were imminent.

Regulatory Issues. From a regulatory standpoint, the Food and Drug Administration (FDA) considers that a pandemic flu vaccine produced using currently-approved processes would merely represent a strain change (as with seasonal flu vaccine), not a new product.⁸² This would allow for a streamlined approval process in which a licensed manufacturer would submit additional information as a supplement to its current product license. The agency considers that virus derived by reverse genetics or grown using cell culture methods does not pose

⁷⁹ See White House Office of Management and Budget, Estimate No. 15, Nov. 1, 2005, at [http://www.whitehouse.gov/omb/budget/amendments/supplemental_11_01_05.pdf].

⁸⁰ Testimony of HHS Secretary Michael Leavitt before the Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, hearing on “Pandemic Flu,” Nov. 2, 2005, 109th Congress, 1st Sess.

⁸¹ See Fedson article. The author also comments that the United States has been ahead of other countries in providing public funding to support the development of prototype pandemic vaccines.

⁸² Presentation of Jesse L. Goodman, Director, FDA Center for Biologics Evaluation and Research, “Meeting the Challenge of Pandemic Vaccine Preparedness: An FDA Perspective,” at the Institute of Medicine Symposium on Pandemic Influenza Research, Apr. 5, 2005, at [<http://www.iom.edu/project.asp?id=25218>]. See also Jennifer Corbett Dooren, “FDA Aims to Approve New Flu Treatments in Weeks,” Dow Jones News Service, Nov. 4, 2005.

additional regulatory obstacles.⁸³ Prototype human vaccines ideally should undergo clinical trials to establish efficacy, dosage and scheduling protocols. The FDA recommends that these trials be carried out before any pandemic occurs, to the extent possible.

The National Institutes of Health (NIH) has awarded contracts to Aventis Pasteur (now sanofi pasteur) to develop prototype human vaccines against H5N1 flu, and to Chiron Corporation to develop vaccines against H5N1 as well as H9N2 flu.⁸⁴ Clinical trials of these vaccines are ongoing, under NIH supervision.

The HHS final plan notes that if a pandemic were to spread swiftly, pandemic vaccine may be pressed into service before standard safety and efficacy tests could be completed. Such unlicensed vaccine could be used under FDA's Investigational New Drug (IND) provisions. These include strict inventory control, record keeping, and informed consent requirements, which would pose an additional challenge for public health officials during a vaccination campaign.

Congress provided an additional mechanism, permitting the use of unapproved drugs and vaccines in an emergency, in the Project BioShield Act of 2004 (P.L. 108-276). This *Emergency Use Authorization* (EUA) permits the use of unapproved products during a declared public health emergency when alternatives are not available.⁸⁵ In early 2005, when FDA issued an EUA for an anthrax vaccine for the military, the agency noted that the statute is self-executing, and that implementing regulations were not required.⁸⁶

Liability and Compensation. Certain vaccines are covered under the National Vaccine Injury Compensation Program (VICP). Under VICP, an excise tax applied to vaccine sales pays for a public compensation fund. Congress enacted the program in 1986 as a no-fault alternative to the tort system for resolving personal injury claims resulting from adverse reactions to recommended childhood vaccines. Individuals of any age alleging injury from any covered vaccine must seek compensation through the program first, though they may decline a proposed award

⁸³ Reverse genetics is a technique to modify viruses so they can be grown more easily for vaccine production. Cell culture is a streamlined method of growing large amounts of virus. Both techniques are explained in greater detail in CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by Sarah A. Lister and Erin D. Williams.

⁸⁴ See NIH: National Institute of Allergy and Infectious Diseases influenza page at [<http://www.niaid.nih.gov/dmid/influenza/>]; and Pandemic Influenza Preparedness Program page, at [<http://www.niaid.nih.gov/dmid/influenza/panintro.htm>].

⁸⁵ FDA, "Emergency Use Authorization of Medical Products," draft guidance, not for implementation, June 2005, at [<http://www.fda.gov/cber/gdlns/emeruse.pdf>]. The authority to declare an emergency authorizing this use is also provided in P.L. 108-276, and is somewhat broader than the HHS Secretary's public health emergency authority.

⁸⁶ FDA, "Authorization of Emergency Use of Anthrax Vaccine Adsorbed for Prevention of Inhalation Anthrax by Individuals at Heightened Risk of Exposure Due to Attack With Anthrax; Availability," 70 *Federal Register* 5452, Feb. 2, 2005.

and then seek a remedy in court.⁸⁷ Congress added *trivalent* flu vaccine (the annual vaccine that contains three strains) to the VICP list in the American Jobs Creation Act of 2004 (P.L.108-357). Since the law explicitly covered trivalent vaccine, *monovalent* (or single-strain) pandemic vaccines would not be covered under VICP. Mechanisms to indemnify manufacturers and officials involved in a pandemic flu vaccine campaign, and to compensate those who may be injured by a monovalent pandemic vaccine, do not exist at this time.

Important lessons from the smallpox vaccination program in 2003 and the swine flu scare in 1976 inform policy discussions about liability and compensation today.

During implementation of the smallpox vaccination program, Congress grappled with the task of waiving liability in order to protect the manufacturer, public officials, health providers and others who would make, recommend and deliver the product, while assuring that those who suffered adverse events resulting from the vaccine could be appropriately compensated.⁸⁸ The smallpox vaccine used for the 2003 campaign carries an unusually high risk of adverse events, and most scientists do not believe that a pandemic flu vaccine would carry a comparable risk.

Nonetheless, public health officials recall the outcome of the swine flu campaign in 1976, an event that is often called a debacle.⁸⁹ In January 1976, a novel influenza strain (“swine flu”) emerged in New Jersey. In March, the Ford Administration announced a campaign to vaccinate the U.S. population by December. On August 18, Congress passed P.L. 94-380, the National Swine Flu Immunization Program of 1976. Among other provisions, the law shielded manufacturers, distributors, and public or private organizations that would administer the vaccine from claims of injury or death that might result, and established that all such claims would be asserted directly against the United States. More than 40 million civilians were vaccinated against swine flu between October 1 and December 16. The campaign was suspended at that time due to several findings of a severe neurological condition, causing paralysis and sometimes death, suspected to have been caused by the vaccine. Meanwhile, a flu pandemic never emerged. The worrisome virus from New Jersey never led to a global pandemic, or even to localized outbreaks. The federal government ultimately paid out \$93 million to individuals injured by the vaccine.⁹⁰

⁸⁷ For more information, see the National Vaccine Injury Compensation Program Home Page at [<http://www.hrsa.gov/osp/vicp/INDEX.HTM>].

⁸⁸ See CRS Report RL31960, *Smallpox Vaccine Injury Compensation*, by Susan Thaul.

⁸⁹ Sources for this section are: Richard E. Neustadt and Harvey V. Fineberg, *The Swine Flu Affair*, a report to the Secretary of Health, Education and Welfare, June, 1978; and HHS Draft Pandemic Influenza Preparedness and Response Plan, Annex 11: “Lessons Learned from the 1976 Swine Influenza Program,” Aug. 2004.

⁹⁰ U.S. Department of Justice, Civil Division, Torts Branch, “Swine Flu Statistics,” Jan. 3, 1991. Overall, 4,179 claims were filed under the act. Not all claims were resolved administratively, and 1,604 claimants proceeded to file suit.

Analysts have commented that delays in indemnifying manufacturers threatened the availability of swine flu vaccine in 1976, while delays in providing for injury compensation compromised voluntary participation in the smallpox vaccine campaign in 2003. A successful emergency vaccination campaign may depend on resolving both policy concerns expediently. Several bills have been introduced thus far in the 109th Congress to address liability and/or compensation related to the use of a vaccine developed to prevent pandemic influenza. One measure, the Biodefense and Pandemic Vaccine and Drug Development Act of 2005 (S. 1873), was reported by the Senate Committee on Health, Education, Labor, and Pensions. Others, such as S. 1880 and companion bills S. 1437 and H.R. 3970, have not been acted upon. On November 1, 2005, HHS Secretary Leavitt transmitted to Congress a draft bill that would provide limited immunity to persons involved in the manufacture and administration of a pandemic vaccine. The draft bill does not contain provisions for compensation of persons who may be injured by the product.⁹¹

Intellectual Property Issues. To produce a vaccine against H5N1 or another pandemic flu strain, scientists start with a virus in circulation, and modify it for mass production. Flu virus for vaccine is grown in fertilized chicken eggs. Avian flu strains must first be weakened, or *attenuated*, or they would kill the chicken embryos. Typically, flu viruses are attenuated using a cumbersome trial-and-error gene swapping process. In developing prototype H5N1 vaccines, the virus was attenuated using a process called *reverse genetics* (RG). RG is a more efficient and reliable means of genetic modification, which removes unwanted genes and substitutes others.

RG is a patented invention. One of the patent holders has waived compensation for production of prototype pandemic flu vaccines and clinical trials. Compensation would have to be paid once a pandemic flu vaccine were to enter commercial production. In the United States, the federal government may use patented processes without consent, as long as the patent holder is appropriately compensated.⁹² The situation is more complicated in other countries with vaccine plants (mainly in Europe), and would require that certain agreements among RG patent holders and governments be ironed out before mass production could begin.⁹³

Use of RG speeds the process of strain selection, and its patent is not felt to be a substantial obstacle to the development of pandemic flu vaccine in the United States. RG could simplify the production of flu vaccine for seasonal use, too, but there the patent may be an obstacle. Annual flu vaccine is an inexpensive product with a small profit margin. Its limited market attractiveness is cited as one reason for the pharmaceutical industry's limited interest in making it. Some are concerned that the market for annual flu vaccine would not bear the added cost of royalties, and that

⁹¹ Letter from HHS Secretary Michael Leavitt to House Speaker Dennis Hastert regarding the draft bill, "Pandemic Flu Countermeasure Liability Protection Act," Nov. 1, 2005.

⁹² See CRS Report RL32051: *Innovation and Intellectual Property Issues in Homeland Security*, by John R. Thomas. This authority is based in existing law and does not require an emergency declaration or other special circumstance.

⁹³ See Fedson article.

as a result, improved technologies are not incorporated.⁹⁴ Since pandemic vaccine would be made on the existing seasonal flu vaccine infrastructure, this potential obstacle to enhanced seasonal capacity may hamper pandemic preparedness. A similar problem may exist with respect to upgrading the system to use cell culture growth methods instead of eggs.

Antiviral Drug Supply and Use

Since pandemic flu vaccine would be unavailable in the early stages of a pandemic, governments and private parties have been interested in drugs that could treat or prevent serious illness from flu. Because influenza is a virus, antibiotics, which treat bacterial infections, are not effective in treating the direct effects of flu. Two types of antiviral drugs have been developed to treat flu: *adamantanes* and *neuraminidase inhibitors* (NIs).⁹⁵ Though both types are used to treat serious infections of seasonal influenza, the H5N1 flu strain has been shown to be resistant to adamantanes. Hence, planning efforts for a possible H5N1 pandemic have focused on NIs. Two NIs are available, and both are licensed by the FDA: oseltamivir (Tamiflu®) and zanamivir (Relenza®). The drugs can be used either for treatment when someone is severely ill with flu, or for prevention in those at risk of severe illness. When used for prevention (also called *prophylaxis*), the drugs must be given for weeks (rather than the five-day treatment regime), as long the flu virus is in circulation. This has implications for stockpiling and for the potential development of viral resistance to the drugs.

In June 2005, it was reported that farmers in China were using the flu antiviral drug amantadine (an adamantane) to treat poultry flocks to prevent avian flu, and that this may have caused the H5N1 strain to become resistant to the drug.⁹⁶ Health officials in China and elsewhere denounced the practice. Tamiflu, the more widely available of the two NIs, is thought to be effective against H5N1 flu, but clinical data are limited. As yet, only one case of Tamiflu resistance has been documented in a human H5N1 patient. Scientists caution, though, that resistance could become a greater problem if the drug were pressed into service during an influenza pandemic, especially if it were used for prolonged periods for prophylaxis.⁹⁷ Tamiflu resistance has been documented in strains of seasonal influenza that circle the globe each year.

WHO has recommended that countries create stockpiles of NIs to prepare for a pandemic. Tamiflu, which is patent protected until 2016, holds the bulk of the global market share for NIs and has been stockpiled by several nations. The drug company Hoffman-La Roche Inc. (“Roche”) is the sole maker of Tamiflu, which it produces in a single plant in Switzerland. The company president has testified that

⁹⁴ Ibid.

⁹⁵ See CDC, antivirals for influenza at [<http://www.cdc.gov/flu/professionals/treatment/>].

⁹⁶ See, for example, Fu Jing, “Misuse of antiviral on poultry must stop,” *China Daily*, June 21, 2005, at [http://www.chinadaily.com.cn/english/doc/2005-06/21/content_453023.htm].

⁹⁷ Q. Mai Le, “Avian Flu: Isolation of Drug-resistant H5N1 Virus,” *Nature* 437, 1108 Oct, 20, 2005; and Luciana L. Borio and John G. Bartlett, “Isolation of H5N1 Influenza Virus Resistant to Oseltamivir,” *Clinician’s Biosecurity Network Weekly Bulletin*, Oct. 18, 2005.

the drug takes about 8 to 12 months to produce and has a few production bottlenecks, including a unique natural starter chemical available only in China, and a potentially explosive step that must be carried out in specialized and costly facilities.⁹⁸ He also testified that Roche produced 1.7 million courses of treatment for the 2004-2005 flu season and was working to increase capacity by simplifying production methods, expanding its Swiss facility, and building a second facility in the United States.

Government and private purchases have increased to the point that global production capacity for Tamiflu has been exceeded, and orders are now backlogged. Under pressure to allow other companies to make the drug, Roche had previously asserted that because production was so complicated, the company had not been approached by other interested producers. This has recently changed. The company now reports that it has had many such inquiries, and that it has granted some licenses to allow other manufacturers to make the drug.⁹⁹ In addition, the company announced on October 27, 2005, that it would suspend shipments of Tamiflu to non-government U.S. purchasers, to prevent hoarding of the drug by individuals.¹⁰⁰

Several countries have stockpiled enough Tamiflu to treat one-fifth or more of their populations. The United States has stockpiled 4.3 million treatment courses (enough for about 1.5 percent of the population), with some additional amounts pending delivery.¹⁰¹ The U.S. stockpile of antiviral drugs is maintained in the Strategic National Stockpile (SNS) of drugs, vaccines, antidotes, medical supplies and other measures which may be needed in a public health emergency. The SNS is managed by CDC.

The HHS final pandemic plan proposes that HHS will stockpile enough antiviral drugs to treat 25% of the U.S. population.¹⁰² Per HHS Secretary Leavitt, emergency supplemental funds requested by the President would be used to meet, by the summer of 2007, “the national goal of having available 81 million courses of antivirals, which would be sufficient to treat 25 percent of the U.S. population (75 million courses) and a reserve supply (6 million courses) that could be used to contain an initial U.S.

⁹⁸ Statement of George B. Abercrombie, President and Chief Executive Officer, Hoffman-La Roche Inc., before the Committee on Government Reform, U.S. House of Representatives, hearing on “The Next Flu Pandemic: Evaluating U.S. Readiness,” June 30, 2005, 109th Congress, 1st Sess.

⁹⁹ Roche, “Tamiflu Facts and Figures,” Oct. 27, 2005, at [http://www.roche.com/home.html]. See also, Andrew Pollack, “Is a Bird Flu Drug Really So Vexing?” *The New York Times*, Nov. 5, 2005.

¹⁰⁰ See “Shipments of Flu Drug Suspended: Tamiflu Maker Moves to Foil Hoarding, Meet Winter Demand,” *The Washington Post*, Oct. 28, 2005.

¹⁰¹ Testimony of CDC Director Julie Gerberding before the Senate Committee on Foreign Relations, hearing on “Avian Influenza — Are We Prepared?” Nov. 9, 2005, 109th Congress, 1st Sess.

¹⁰² The NVAC had recommended stockpiling of antiviral drugs sufficient to treat 13% of the population as the minimal requirement, and that amounts sufficient for 45% of the population would be optimal.

outbreak.”¹⁰³ Leavitt said that states were expected to procure 31 million of these courses, for which HHS would reimburse 25 percent of the cost. He stressed the importance of this aspect of state involvement in pandemic preparedness. Some public health officials and Members of Congress protested about the proposed 75 percent state matching requirement, saying that it added an extra burden on top of a proposed \$130 million cut in state public health preparedness grants for FY2006.¹⁰⁴

Priority groups for antiviral drugs are laid out in the HHS final pandemic plan, beginning with treatment for those who are admitted to hospitals with severe illness from flu. Priority categories are otherwise fairly similar to those for vaccine (See **Table 2.**) encompassing certain groups of high risk individuals as well as healthcare workers and other responders.

Public health officials have cautioned against an over-reliance on antiviral drugs in planning, in part because there will be limited availability, but also because it has not been clearly demonstrated that treatment with Tamiflu, for example, would actually improve survival rates in clinical settings during a potential H5N1 pandemic. Nonetheless, given that the best pandemic response tool — vaccine — will be largely unavailable in the early going, governments can offer antiviral drug stockpiling as a tangible effort to protect their citizens.

Influenza as a Weapon

In the late 1990s, Congress authorized the Select Agent program to track the movement of certain bacteria and viruses that could potentially be used as bioterrorist weapons.¹⁰⁵ The program, which is administered by CDC and the U.S. Department of Agriculture, was expanded in statute following the anthrax attacks of 2001. An interagency working group determines which pathogens to place on the list of Select Agents. Once an organism is listed, those individuals and facilities working with it must be registered, undergo background investigations, and follow various guidelines in facility maintenance and management, shipping, recordkeeping and other practices. The list does not include common human strains of influenza, though it does include highly pathogenic strains of avian influenza, i.e., any strains which are shown to cause disease in commercial poultry. As such, H5N1 influenza is a covered pathogen. When scientists from the CDC and the Armed Forces Institute of Pathology recently re-created the 1918 pandemic flu virus, since it was a human influenza virus, it was not on the Select Agent list. It was subsequently added by

¹⁰³ Testimony of HHS Secretary Michael Leavitt before the Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, hearing on “Pandemic Flu,” Nov. 2, 2005, 109th Congress, 1st Sess.

¹⁰⁴ See Gardiner Harris, “Administration’s Flu Plan Gets Mixed Reception in Congress,” *The New York Times*, Nov. 3, 2005.

¹⁰⁵ For more information, see the CDC Select Agent program page at [<http://www.cdc.gov/od/sap>] and CRS Report RL31719, *An Overview of the U.S. Public Health System in the Context of Emergency Preparedness*, by Sarah A. Lister.

HHS Secretary Leavitt on October 20, 2005.¹⁰⁶ Other flu strains which typically affect humans (rather than birds) remain unregulated at this time.

The matter of whether influenza viruses could be used deliberately as biological weapons has received recent attention in Congress. When asked about the possibility, CDC Director Julie Gerberding replied that "... we recognize that influenza has some of the important characteristics of an excellent threat agent. It's easily transmissible, it's relatively easy to produce and it's very easy to modify or engineer. So it does have characteristics that if a person was intent on modifying ..., it is not beyond our imagination to consider that beyond our preparedness efforts."¹⁰⁷ Dr. Gerberding also noted the natural behavior of the virus, which constantly shuffles its genes to produce new combinations, saying that "mother nature herself is a very effective terrorist.

¹⁰⁶ CDC, "Possession, Use, and Transfer of Select Agents and Toxins - Reconstructed Replication Competent Forms of the 1918 Pandemic Influenza Virus Containing Any Portion of the Coding Regions of All Eight Gene Segments," 70 *Federal Register* 61047, Oct. 20, 2005.

¹⁰⁷ Testimony of CDC Director Julie Gerberding before the House Committee on Homeland Security, Subcommittee on Prevention of Nuclear and Biological Attacks, hearing on "National Biodefense Strategy," July 28, 2005, 109th Congress, 1st Sess.